

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**

What is claimed is:

1. A substantially pure polypeptide characterized as:
 - (a) modulating intracellular glutamate transport;
 - (b) interacting with a glutamate transporter protein; and
 - (c) having an expression pattern in the brain.
2. The polypeptide of claim 1, wherein the glutamate transporter protein is EAAT4.
3. The polypeptide of claim 1, wherein the modulation is an increase in glutamate transport.
4. The polypeptide of claim 1, wherein the polypeptide is further characterized as:
 - (a) having at least one PDZ domain;
 - (b) having at least one regulatory G-protein domain;
 - (c) having at least one pleckstrin homology domain;
 - (d) having at least one proline-rich domain; and
 - (e) having at least one guanine exchange factor domain.
5. The polypeptide of claim 1, wherein the polypeptide is further characterized by
 - (a) having at least one pleckstrin homology domain;
 - (b) having at least one spectrin repeat; and
 - (c) having at least one α -actinin domain.
6. The polypeptide of claim 1, wherein the expression pattern is in Purkinje cells.
7. The polypeptide of claim 1, wherein the polypeptide has an amino acid sequence as set forth in SEQ ID NO:2.
8. The polypeptide of claim 1, wherein the polypeptide has an amino acid sequence as set forth in SEQ ID NO:4.
9. A substantially pure polypeptide having an amino acid sequence as set forth in SEQ ID NO:2, or conservative variants thereof.

- Cont
BS
10. A substantially pure polypeptide having an amino acid sequence as set forth in SEQ ID NO:4, or conservative variants thereof.
11. An isolated polynucleotide encoding a polypeptide according to claim 1.
12. An isolated polynucleotide selected from the group consisting of:
- a polynucleotide encoding a polypeptide having an amino acid sequence as set forth in SEQ ID NO:2;
 - a polynucleotide of (a), wherein T can be U;
 - a polynucleotide complementary to (a) or (b);
 - a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:1;
 - degenerate variants of (a), (b), (c) or (d); and
 - a fragment of (a), (b), (c), (d) or (e) having at least 15 base pairs and hybridizes to a polynucleotide encoding a polypeptide as set forth in SEQ ID NO:2.
13. An isolated polynucleotide selected from the group consisting of:
- a polynucleotide encoding a polypeptide having an amino acid sequence as set forth in SEQ ID NO:4;
 - a polynucleotide of (a), wherein T can be U;
 - a polynucleotide complementary to (a) or (b);
 - a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:3;
 - degenerate variants of (a), (b), (c) or (d); and
 - a fragment of (a), (b), (c), (d) or (e) having at least 15 base pairs and hybridizes to a polynucleotide encoding a polypeptide as set forth in SEQ ID NO:4.
14. An antibody that binds to a polypeptide of claim 7 or 8 or binds to immunoreactive fragments thereof.
15. The antibody of claim 14, wherein the antibody is polyclonal.
16. The antibody of claim 14, wherein the antibody is monoclonal.

- Cont
BS*
17. The antibody of claim 14, wherein the antibody disrupts interaction of the polypeptide with a glutamate transporter protein.
 18. An expression vector comprising a polynucleotide of claim 11.
 19. The expression vector of claim 18, wherein the vector is virus-derived.
 20. The expression vector of claim 18, wherein the vector is plasmid-derived.
 21. A host cell comprising a vector of claim 18.
 22. A method for producing a polypeptide comprising the steps of:
 - (a) culturing a host cell of claim 21 under conditions suitable for the expression of the polypeptide; and
 - (b) recovering the polypeptide from the host cell culture.
 23. A substantially pure polypeptide, wherein the polypeptide interacts with amino acid sequence QEAELTLP (SEQ ID NO:9) or amino acid sequence GRGGNESVM (SEQ ID NO:10).
 24. A polynucleotide encoding the polypeptide of claim 23.
 25. A substantially pure polypeptide, wherein the polypeptide interacts with the amino acid sequence set forth in SEQ ID NO:12.
 26. A substantially pure polypeptide, wherein the polypeptide interacts with the amino acid sequence set forth in SEQ ID NO:13.

27. A method for identifying a compound that modulates a cellular response mediated by a Glutamate Transporter Associated Protein comprising:
- (a) incubating the compound with a cell expressing a Glutamate Transporter Associated Protein and a glutamate transporter protein under conditions sufficient to permit the components to interact
 - (a) comparing a cellular response in the cell incubated with the compound with the cellular response of a cell not incubated with the compound;
- thereby identifying a compound that modulates a cellular response mediated by a Glutamate Transporter Associated Protein .
28. The method of claim 27, wherein the cellular response is an increase in glutamate transport.
29. The method of claim 27, wherein the cellular response is a decrease in glutamate transport.
30. The method of claim 27, wherein the cellular response is an increase in cytoskeletal stability.
31. The method of claim 27, wherein the cellular response is a decrease in cytoskeletal stability.
32. The method of claim 27, wherein the cellular response is an increase in chloride flux.
33. The method of claim 27, wherein the cellular response is a decrease in chloride flux.
34. The method of claim 27, wherein the Glutamate Transporter Associated Protein is selected from the group consisting of GTRAP4-41, GTRAP4-48, PCTAIRE-1 and GTRAP3-18.
- Cont
BS*

- Cont
p5*
35. The method of claim 27, wherein the glutamate transport protein is selected from the group consisting of GLAST, GLT-1, EAAC1, EAAT1, EAAT1, EAAT2, EAAT3, EAAT4 and EAAT5.
 36. The method of claim 27, wherein the glutamate transport protein is EAAT4 and the Glutamate Transporter Associated Protein is GTRAP4-41, GTRAP4-48 or PCTAIRE-1.
 37. The method of claim 27, wherein the glutamate transport protein is EAAC1 and the Glutamate Transporter Associated Protein is GTRAP3-18.
 38. The method of claim 27, wherein the cell further expresses a RhoGEF protein.
 39. The method of claim 27, wherein the compound is selected from the species consisting of a peptide, a peptidomimetic, a polypeptide, a pharmaceutical, a chemical compound, a biological agent and an antibody.
 40. The method of claim 27, wherein the cell is selected from the group consisting of a neuronal cell, a glial cell, a cardiac cell, a bronchial cell, a uterine cell, a testicular cell, a liver cell, a renal cell, an intestinal cell, a thymus cell, a spleen cell, a placental cell, a skeletal muscle cell and a smooth muscle cell.
 41. A method for identifying a compound that inhibits an interaction between a Glutamate Transporter Associated Protein and a glutamate transporter protein comprising:
 - (a) contacting a Glutamate Transporter Associated Protein with a glutamate transporter protein in the presence of the compound and
 - (b) comparing the formation of a Glutamate Transporter Associated Protein-glutamate transporter protein complex in the presence of the compound with a formation of the complex in the absence of the compound,
thereby identifying a compound that inhibits an interaction between a Glutamate Transporter Associated Protein and a glutamate transporter protein.

- Cont
BS*
42. The method of claim 41, wherein the Glutamate Transporter Associated Protein is selected from the group consisting of GTRAP4-41, GTRAP4-48, PCTAIRE-1 and GTRAP3-18.
 43. The method of claim 41, wherein the glutamate transport protein is selected from the group consisting of GLAST, GLT-1, EAAC1, EAAT1, EAAT1, EAAT2, EAAT3, EAAT4 and EAAT5.
 44. The method of claim 41, wherein the glutamate transport protein is EAAT4 and the Glutamate Transporter Associated Protein is GTRAP4-41, GTRAP4-48 or PCTAIRE-1.
 45. A method of treating a disorder associated with glutamate transport comprising administering to a subject in need thereof a therapeutically effective amount of a compound that modulates a Glutamate Transporter Associated Protein activity or interaction with a glutamate transporter protein.
 46. The method of claim 45, wherein the Glutamate Transporter Associated Protein is GTRAP4-41, GTRAP4-48 or PCTAIRE-1 .
 47. The method of claim 46, wherein the disorder is a disorder of the nervous system.
 48. The method of claim 47, wherein the disorder of the nervous system is neurodegeneration, Spinocerebellar ataxia type 1 (SCA1), or schizophrenia.
 49. The method of claim 45, wherein the Glutamate Transporter Associated Protein is GTRAP3-18.
 50. The method of claim 49, wherein the disorder is epilepsy or a disorder of GABA metabolism or schizophrenia.
 51. The method of claim 45, wherein the compound is selected from the species consisting of a peptide, a peptidomimetic, a polypeptide, a pharmaceutical, a chemical compound, a biological agent and an antibody.

- Cont
BS*
52. A method of treating a disorder associated with chloride flux comprising administering to a subject in need thereof a therapeutically effective amount of a compound that modulates a Glutamate Transporter Associated Protein activity or interaction with a glutamate transporter protein.
 53. The method of claim 52, wherein the Glutamate Transporter Associated Protein is GTRAP4-41, GTRAP4-48, PCTAIRE-1 or GTRAP3-18.
 54. The method of claim 52, wherein the disorder is a disorder of the nervous system.
 55. A method of modulating glutamate transport in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of a compound that modulates expression of a Glutamate Transporter Associated Protein, thereby modulating glutamate transport.
 56. The method of claim 55, wherein the Glutamate Transporter Associated Protein is GTRAP3-18.
 57. The method of claim 55, wherein the compound is a polynucleotide having a nucleic acid sequence substantially similar to SEQ ID NO:20. (5'-GAGCGGGCAAGGTTCAC-3')
 58. The method of claim 55, wherein the compound is retinoic acid.
 59. The method of claim 56, wherein the modulation of glutamate transport is a decrease in glutamate transport.
 60. The method of claim 55, wherein the Glutamate Transporter Associated Protein is GTRAP4-41, PCTAIRE-1 or GTRAP4-48.
 61. The method of claim 60, wherein the modulation of glutamate transport is a increase in glutamate transport.

- Cont
35*
62. A transgenic non-human animal having a transgene that expresses a polypeptide of claim 1 chromosomally integrated into the germ cells of the animal.
 63. The transgenic animal of claim 62, wherein the animal is murine.
 64. A transgenic non-human animal whose genome comprises a disruption of a Glutamate Transporter Associated Protein gene, wherein the disruption comprises the insertion of a transgene comprising a selectable marker sequence, and wherein the disruption results in a disorder of the nervous system as compared to a wild-type animal not having the disruption.
 65. A transgenic animal according to claim 64, wherein the disorder of the nervous system is selected from the group consisting of a disorder of glutamate transport, neurodegeneration, epilepsy, glutamate toxicity, disorders of memory, disorders of learning, Alzheimer's disease, cerebellar degenerative disease, spinocerebellar ataxia type 1, Huntington's disease, perinatal hypoxia, amyotrophic lateral sclerosis and alcoholic brain injury.
 66. A transgenic animal of claim 64, wherein said animal is heterozygous or homozygous for the disruption of the endogenous Glutamate Transporter Associated Protein gene.

- Cont
BS*
67. A method for producing a transgenic mouse exhibiting a disorder of the nervous system, said method comprising:
- (a) introducing a transgene comprising a selectable marker sequence into a mouse embryonic stem cell;
 - (b) introducing the mouse embryonic stem cell into a mouse embryo;
 - (c) transplanting the embryo into a pseudopregnant mouse; allowing the embryo to develop to term; and
 - (d) identifying a transgenic mouse whose genome comprises a disruption of the endogenous Glutamate Transporter Associated Protein gene, wherein the disruption results in the mouse exhibiting a disorder of the nervous system as compared to a wild-type mouse.
68. A method according to claim 67, wherein the transgenic mouse is homozygous for the disruption of the endogenous Glutamate Transporter Associated Protein gene.
69. A method according to claim 67, wherein the transgenic mouse is heterozygous for the disruption of the endogenous Glutamate Transporter Associated Protein gene.
70. A computer readable medium having stored thereon a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, and sequences substantially identical thereto, or a polypeptide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, and sequences substantially identical thereto.

- Cont
75*
71. A computer system comprising a processor and a data storage device wherein said data storage device has stored thereon a nucleic acid sequence selected from the group consisting of SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and sequences substantially identical thereto, or a polypeptide sequence selected from the group consisting SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and sequences substantially identical thereto.
 72. The computer system of claim 71, further comprising a sequence comparison algorithm and a data storage device having at least one reference sequence stored thereon.
 73. The computer system of claim 71, wherein the sequence comparison algorithm comprises a computer program which indicates polymorphisms.
 74. The computer system of claim 71, further comprising an identifier which identifies features in said sequence.
 75. A method for comparing a first sequence to a reference sequence wherein said first sequence is a nucleic acid sequence selected from the group consisting SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5 and sequences substantially identical thereto, or a polypeptide sequence selected from the group consisting of SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and sequences substantially identical thereto comprising:
 - (a) reading the first sequence and the reference sequence through use of a computer program which compares sequences; and
 - (b) determining differences between the first sequence and the reference sequence with the computer program.
 76. The method of claim 75, wherein determining differences between the first sequence and the reference sequence comprises identifying polymorphisms.

- Cmt
35*
77. A method for identifying a feature in a sequence wherein the sequence is selected from the group consisting of a nucleic acid sequence SEQ ID NO:1, SEQ ID NO:3, SEQ ID NO:5, sequences substantially identical thereto, or a polypeptide sequence SEQ ID NO:2, SEQ ID NO:4, SEQ ID NO:6 and sequences substantially identical thereto comprising:
- reading the sequence through the use of a computer program which identifies features in sequences; and
 - identifying features in the sequences with the computer program.
78. A substantially pure polypeptide characterized as:
- modulating intracellular glutamate transport;
 - interacting with a glutamate transporter protein;
 - having an expression pattern in neural non-neuronal tissues;
 - having at least one kinase C domains;
 - having four transmembrane domains; and
 - being hydrophobic.
79. The polypeptide of claim 78, wherein the glutamate transporter protein is EAAC1.
80. The polypeptide of claim 78, wherein the modulation is a decrease in glutamate transport.
81. The polypeptide of claim 78, wherein the polypeptide has an amino acid sequence as set forth in SEQ ID NO:6.
82. A substantially pure polypeptide having an amino acid sequence as set forth in SEQ ID NO:6, or conservative variants thereof.
83. An isolated polynucleotide encoding a polypeptide according to claim 78.

84. An isolated polynucleotide selected from the group consisting of:
- (a) a polynucleotide encoding a polypeptide having an amino acid sequence as set forth in SEQ ID NO:6;
 - (b) a polynucleotide of (a), wherein T can be U;
 - (c) a polynucleotide complementary to (a) or (b);
 - (d) a polynucleotide having a nucleotide sequence as set forth in SEQ ID NO:5;
 - (e) degenerate variants of (a), (b), (c) or (d); and
 - (f) a fragment of (a), (b), (c), (d) or (e) having at least 15 base pairs and hybridizes to a polynucleotide encoding a polypeptide as set forth in SEQ ID NO:6.
85. An antibody that binds to a polypeptide of claim 82 or binds to immunoreactive fragments thereof.
86. The antibody of claim 85, wherein the antibody is polyclonal.
87. The antibody of claim 85, wherein the antibody is monoclonal.
88. The antibody of claim 85, wherein the antibody disrupts interaction of the polypeptide with a glutamate transporter protein.
- Cont
35*